PATENT

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Dated: June 10, 2008 BY: Rodney D. DeKruif

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Emrick et al.	
Serial No: 10/643,015	Attorney Docket No. 7163
Filed: August 18, 2003	
For: PYRIDINE AND RELATED LIGAND COMPOUNDS, FUNCTIONALIZED NANOPARTICULATE COMPOSITES AND METHODS OF PREPARATION	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RULE 131 DECLARATION OF TODD S. EMRICK

1. I, Todd S. Emrick, am an Associate Professor of Chemistry at the University of Massachusetts, Amherst and a co-inventor with regard to the invention (the "Invention") disclosed and claimed in the above-entitled application (the "Application"). I make this declaration in support of the Application and, in particular, to antedate a reference cited against the Application.

2. The Invention claimed in the Application was completed before the effective date of application serial number 10/219,440 (*i.e.*, the Dubertret reference). More specifically, the Invention was conceived and with due diligence reduced to practice, in this country--the United States of America, prior to the effective date of the Dubertret reference.

3. This Declaration, and prior invention, is supported by copies of pertinent pages from the laboratory research notebook of co-inventor Habib Skaff, signed and dated by Mr. Skaff, entries to which I contemporaneously witnessed. Date redacted copies of the aforementioned notebook pages are provided collectively as Exhibit A and incorporated herein by reference. These documents establish that the Invention was made at least as early as June 1, 2002, which is a date earlier than the effective date of the Dubertret reference.

4. More specifically, as part of his graduate research work with me, Dr. Skaff prepared composites of a metallic nanoparticulate component coupled to a polymeric ligand component. For purposes relating to our research, we referred to such a nanoparticulate as a nanocrystal, abbreviated "Nc". Preparation of such a nanoparticulate, Nc, composite is evidenced on page 37 of Exhibit A, and the composite recorded therein was prepared at least as early as June 1, 2002.

(a) Representing a range of available nitrogen-containing moieties, Dr. Skaff used a pyridinyl group to couple the ligand and nanoparticulate components. Coupling of such ligand and nanoparticulate components is

evidenced on page 37 of Exhibit A, and the coupling recorded therein was achieved at least as early as June 1, 2002.

(b) Representing a range of available nanoparticulate components, Dr. Skaff used CdSe. Use of such a nanoparticulate is evidenced on pages 37-38 of Exhibit A, and the nanoparticulate recorded therein was used at least as early as June 1, 2002.

(c) Representing a range of available polymers, Dr. Skaff used poly(ethylene glycol) to prepare such a polymeric ligand component. Preparation of such a ligand component, including coupling to a pyridinyl moiety, is evidenced on pages 14-15, 23, 25 and 37 of Exhibit A, and the ligand recorded therein was prepared at least as early as June 1, 2002.

(d) Representing a range of available terminal functional groups, Dr. Skaff chose a hydroxy group to terminate poly(ethylene glycol). Preparation of such a hydroxy-terminated polymeric ligand component, and subsequent coupling with a nanoparticulate, is evidenced on pages 15 and 37 of Exhibit A, and the ligand recorded therein was prepared and used at least as early as June 1, 2002.

5. As a related part of his graduate research with me, Dr. Skaff also prepared systems for nanoparticulate dispersion. As part of such a system, he prepared a composite of a metallic nanoparticulate component (Nc) and a ligand component in a liquid medium: a representative nanoparticulate component, CdSe, was coupled to a tri-n-octyl phosphine oxide (TOPO) ligand component,

then dissolved in tetrahydrofuran (THF). Preparation of such a composite of a ligand component in a liquid medium is evidenced on page 38 of Exhibit A, and the composite in liquid medium recorded therein was prepared at least as early as June 1, 2002.

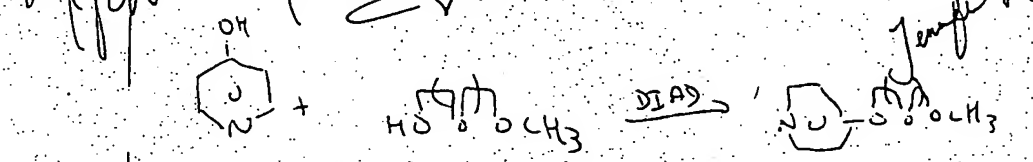
(a) The system Dr. Skaff prepared also included another ligand component in another liquid medium. Representative of many available ligands and as described above, he used a ligand of poly(ethylene glycol) with a pyridinyl coupling moiety and showed this ligand to be soluble in water. Ligand preparation and water solubility is evidenced on page 15 of Exhibit A, and the ligand recorded therein was prepared and dissolved at least as early as June 1, 2002.

(b) To demonstrate this dispersion system, Dr. Skaff precipitated the CdSe-TOPO composites out of THF solution. To demonstrate greater nanoparticulate affinity for another ligand component, the CdSe-TOPO composites were redissolved in a water medium containing pyridinyl/poly(ethylene glycol) ligand components. With dissolution of the nanoparticulates in water, he showed that the pyridinyl/poly(ethylene glycol) ligand components have greater affinity for the CdSe nanoparticulates than the TOPO ligand components. This dispersion system, showing greater nanoparticulate affinity of one ligand component over another, is evidenced on page 38 of Exhibit A, and the system for nanoparticulate dispersion recorded therein was demonstrated at least as early as June 1, 2002.

I hereby declare that: All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; that those statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code; and that willful false statements may jeopardize the validity of the Application or any patent issuing thereon.

Date 6-9-08

Todd S. Emrick



Reagents

95 ①  2g, 0.022mol

②

75 ② m-Pg 750 14.25g, 0.019mol

262 ③ Ph_3P 6.25g, 0.024mol

22 ④ DIAD 4.84g, 0.024mol (4.72mL)

⑤ THF (dry) ~~300mL~~ 250mL

Procedure

① Ph_3P + THF loaded into 2-neck flask & stirred under N_2 @ r.t.

② DIAD added via syring & stirred for ½ hr.

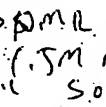
③ phenol & alcohol added & stirred

④ reacted overnight

⑤ stripped off THF

⑥ added 1:1 DI-H$_2$O : ether → washed w/ etc.

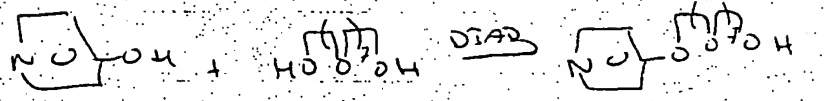
⑦ extracted product out w/ CH_2Cl_2 out of Aq phase → $MgSO_4$, Rotovap

→ NMR show some  → try to recrystallize in ether/hexane

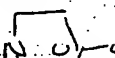
basic (5M NaOH) solution & precipitate into CH_2Cl_2 (cold)

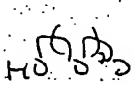
→ run column chromatography w/ CH_2Cl_2 : EtOAc (7:3:0), (7:2:1)

Exhibit A



Reagents

95 ①  & 2g, 0.011mol

400 ρ=1.03 ②  22g, 0.055mol

202 ③ DIAD 2.63g, 2.5mL 0.013mol

262 ④ Ph_3P 3.41g, 0.013

⑤ THF (dry) 300mL

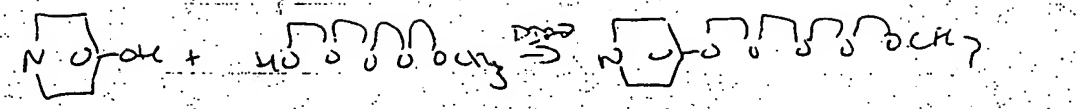
Procedure

① Ph_3P + THF loaded into 3-neck 500mL round bottle
: stirred @ r.t. under N_2

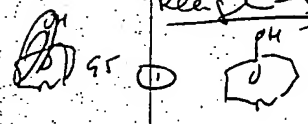
② DIAD added via syring : stirred for ½ hr.

③ phenol : ~~ethanol~~ diol added : stirred
→ reacted overnight

- rotovaped off all THF → note
- extracted w/ H_2O → turn aqueous washed
- w/ CH_2Cl_2 → too difficult to purify by column
- rotovaped off CH_2Cl_2 → dissolved in H_2O,
washed w/ ether, then Toluene → doesn't work well either
- try ~~acidifying~~ acidifying aqueous to make pyridine salt
which will not be soluble in



Reagents



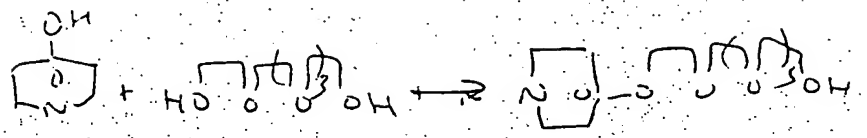
	①	5g,	0.055 g mol
128	② m-T-g	5.632g,	0.044 mol
1.02 26 202	③ Ph_3P	13.1g	0.05 mol
	④ DIAD	10.1g,	0.05 mol, 9.85 mL
	⑤ THF (dry)		400 mL

Procedure

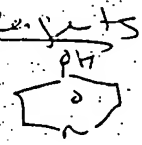
① [redacted] Ph_3P & THF loaded into 2-neck flask & stirred under N_2 g.e.

② DIAD added via syring & stirred for ½ hr.

③ phenol & alcohol added & stirred overnight



Reagents

95 ①		4g, 0.042mol	
300 ②	Hex	31.58g, 0.105mol	
262 ③	Ph_3P	13.1g	~~0.045~~ 0.05mol
(~1.0×) 202 ④	DIAD	10.1g, 0.05mol,	~~10.35mL~~ 9.85mL
⑤	THF	500mL	

Procedure

① phenol, Ph_3P, DIAD, & THF loaded in 2-neck & stirred @ r.t. under N_2 for ½ hr.

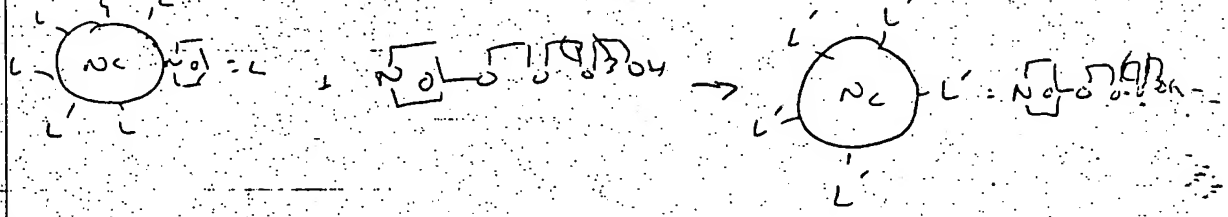
② diol added ⇒ stirred overnight

- stripped of THF
- ⇒ hrs in $CHCl_3$ @ $CHCl_3$: acetone (80:20) ③ ~~ethyl~~ $CHCl_3$: acetone : MeOH (75:20:5)
- ran column eluting w/ ④ $CHCl_3$: acetone : MeOH (7:2:1)
- tried distilling off unreacted diol @ ~~220~~ 224°C @ @ 600 mtorr ⇒ didn't work well
- ran column in $CHCl_3$: acetone : MeOH (75:20:2), (75:20:5), (80:20:10)

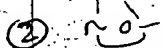
Jennifer L. Lanier

Kate E. Bi

Exchange to hex-monopyridinyl ether



Reagent

1. Pyridine NC ~40mg
2.  600mg
3. THF (dry) 3mL
4. DIW 6mL

Procedure

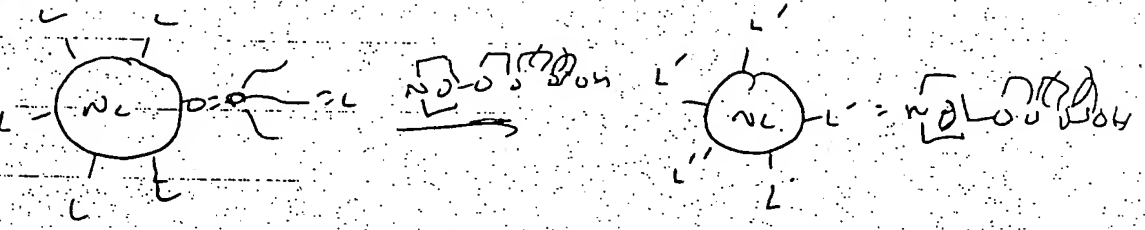
A) ① 20mg NC dispersed in Solution of 300mg new ligand in THF → immediately went into solution

② dried under N_2 flow and added 3mL DIW → most went into solution → centrifuged

B) ③ 20mg NC dispersed in Solution of 300mg new ligand in 3mL DIW → NC went into solution → centrifuged

Jennifer L. Lemmon

Kate Bl



Reagents

1. TOPO covered NC ~15mg
2. NC-COOH 320 mg
3. THF (dry) 3mL

Procedure

1. NC made as usual & washed w/ MeOH 3 times
2. dried over N_2 flow
3. redissolved in new ligand in THF and allowed to stand over head of N_2 overnight
4. distilled at ½ THF → precipitated w/ hexane → all NC precipitated
5. washed w/ hexanes → centrifuged → redissolved in H_2O